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PRESENTATION

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Good afternoon everybody. I am Chris Schott, Pharmaceutical Analyst at JP Morgan, and very pleased to be introducing Pfizer this afternoon. From Pfizer we have Mikael Dolsten, the company’s worldwide President of R&D. Obviously a very eventful start to the year with nice update on palbociclib and I am sure Mikael will run through the broader Pfizer pipeline from there. So let me turn it over.

Mikael Dolsten - Pfizer Inc - President

So I’m excited to be here and give you an update on how we’re advancing differentiated high-value products in the pipeline of Pfizer. Let me remind all of us that the presentation and discussion includes forward-looking statements, actual results may differ from those results expressed or implied during this presentation. For more details, please follow up on our web page.

So over the last couple of years, we’ve had good progress in moving products from our pipeline to the marketplace, last five years we have moved 16 approvals and 10 are NMEs and just a couple of years from 2011 onwards, I have exemplified some of the most important products that are now doing really well, prescribed by physicians, used by patients. And let me illustrate Eliquis, which is now the number one novel oral anticoagulant NOAC among prescribing cardiologists. And we believe the differentiated profile of Eliquis will support its continuous growth as being the preferred brand.

XELJANZ, which is the first oral JAK inhibitor that was available to RA patients is now the third prescribed choice among rheumatologists in the segment of self-administrated biologicals, and is now above 10% of market share in that segment and continue to do well in a number of important markets.

The pipeline contains currently 86 different programs, and I will now be able to share with you a little more insight into some of the exciting new medical entities or new indications that are in our pipeline. We really welcome the opportunity for this discussion, I do think the Pfizer pipeline is somewhat underappreciated and therefore it’s a very timely opportunity to allow you to get a deeper insight into the breadth of mechanisms and new indications that we have over the next few years moving forward, as well as some of the breakthrough science that’s coming in the next wave beyond that.

The pipeline contains programs spread around six different therapeutic areas as well as bio-similars, and a nice mix of small molecules, biologicals and vaccines. Over the next four years, near-term, we project from the pipeline more than 20 potential pivotal registration study starts. And some examples I’ll present here, you can see a significant momentum with several NMEs in oncology, important expansion of new indication in inflammation, new vaccines, new exciting drugs in rare disease and also biosimilar growing portfolio.

Over the next four years, we also project the potential for more than 15 approvals, and you can see that exemplified again with the strong contribution from Oncology, CVMed, Inflammation, Rare Disease and Biosimilars. Please note that these examples exclude potential additional opportunity from our alliance with Merck KGaA around PD-L1 in immuno-oncology, as we will speak more about that alliance and our plans around ASCO and onwards.

When I look at our pipeline, you can in a way, near term, put your hands on six significant growth platforms. In Oncology, we have two around palbociclib and our immuno-oncology activities. We have bococizumab in CVMed and in Vaccines, we have the expansion of the adult vaccine sectors supported from last year by the landmark data, strong results we had for Prevnar 13 Adult in the CAPiTA trial and have indicated that these segments of adult vaccination, we think it’s going to be a growing, a very important segment. And please note that this year we plan also to bring
an expanded serotype pneumococcal vaccines towards the clinic going beyond the certain serotypes and you will hear more about expanding the adult use of vaccine by our exciting staph aureus opportunity. And on the right hand here on the slide you can see a growing biosimilar portfolio supporting our Established Business, with the first three of them in this box already in Phase 3, bevacizumab planned for Phase 3 first half of this year and adalimumab soon having POC data that could support similar Phase 3 starts this year.

For today’s discussion I’ve highlighted 10 areas that I will give brief vignettes to you to showcase some of the progress and excitement we see in these products.

First of all as a start, IBRANCE, which is the new name for palbociclib and as you are well aware of, it is in priority review for registration and the FDA announced that they have no plans for an advisory community and then instead initiated early labeling discussions with us.

We are very excited about palbociclib, its strong efficacy and very favorable safety profile and look forward to the potential to bring it as soon as possible to the marketplace to women suffering from estrogen receptor-positive breast cancer. Initial indication will be for advanced breast cancer. But please note the great momentum we have in the palbociclib area on this slide, which follows later this year, data release from Phase 3 studies in recurrent breast cancer followed by the full dataset in 2016 in advanced additional combination data from recurrent in 2017. Then moving into early breast cancer of high or medium-risk patients and that’s really the stage when you cure patients and provide tremendous value.

I’m also excited to share with you that we now have some 10 different Phase 1 and Phase 2 studies ongoing outside breast cancer. And this includes lung, head and neck, melanoma, pancreas and a few other indications. And we have invested heavily in the area around CDK 4/6 over the last couple of years and been able to understand the molecular signatures and the type of preclinical data that supports the strategy in the clinic to understand which indications are likely to succeed and how do you combine palbociclib optimally to get the probability of the best response.

So this is a really comprehensive program and I feel proud for Pfizer’s pioneering approach around CDK 4/6 that really sets us apart and make us by significant time advance a leader in this area going forward. A second growth platform for us is immuno-oncology. And together with my colleague Albert Bourla from the VOC unit we have put a lot of efforts to build a growing platform for us. You heard about the alliance we’ve made with Merck KGaA, which allowed us to accelerate our anchor PD-L1 drug by more than two years.

And we, this year are planning to start more than 20 clinical studies -- which up to -- up to 20 clinical studies of which up to six studies we are exploring as pivotal registration in 10 studies. And we’re looking at lung, ovarian, gastric, renal, blood, head and neck among the indications.

As we aspire to be in certain of these indications among the leading companies, our largest focus going forward is also about the growing opportunity to combine PDL-1, PD-1 drugs with other agents. And this year we’re planning for starting clinical studies together with Inlyta for renal carcinoma, Xalkori for ALK-positive lung cancer, and also second generation ALK/ROS agents. Going forward, there will be numerous combination with other immuno-oncology agents currently in the clinic, 4-1BB,OX-40 starting clinic very soon. And overall you will see by the end of this year that we expect to have five different immuno-oncology agents in the clinic that will grow and may possibly double by 2016. And this is supported by near-term opportunities to bring this type of immuno-oncology to the next level and beyond that we’re expanding our modalities with CAR-T cells together with Cellectis with small molecule modulators together with ITUs as well as a significant effort on bifunctional antibodies to create an industry-leading immuno-oncology effort.

I wanted to highlight one of agents that I mentioned, the next-generation Xalkori and here a single drug therapy. It’s an agent that was designed to have almost 50-fold higher potency versus ALK compared to Xalkori and similar very high potency against all known ALK mutations that occur in patients. It was also designed to have high blood brain permeability and give high brain concentration since unfortunately many lung cancer patients that progress up to half of them have brain metastases.

And this is a particular example here, an image analysis of a patient that progressed Xalkori progress ceritinib, a second ALK inhibitor. As you can see on the left side has three significant brain metastases. After three months of therapy with 3922 [PF-06463922], our new generation ALK inhibitor, you can see an almost complete disappearance of the tumor. We have nice response rate on naive as well as patient progressing on one or several ALK inhibitors and we are now planning for a potential pivotal study start 2015.
The third growth platform is our PCSK9 platform and here exemplified by bococizumab, which now is in large -- in a large Phase 3 program. You can see the graph from our Phase 2b study which showed about 60% reduction of cholesterol in patients already treated with the optimal dose of statins.

We have built in several different -- differentiating properties into the profile of bococizumab and it's in clinical trial programs. Let me exemplify just a couple of them. To the best of our knowledge, we are the only company that have a substantial Phase 3 program focusing on primary prevention. And why is that important? Because there is a growing number of diabetic patients, growing number of chronic kidney disease and peripheral artery disease that are at high risk for cardiovascular events and we have one particular trial aiming to generate important data for physicians and payers in this indication. We also are the only company that so far have initiated a trial in patients above 100 in cholesterol only which would allow us potentially to generate very strong outcome data that again could demonstrate important value of these type of drugs and support patient, physician and pay units. Finally, the initial study was designed with an administration two times per month, but we also have a proprietary partnership with Halozyme, which is the unique formulation that may allow you to give slightly larger amount of antibodies and have prolonged dosing intervals and we're exploring that as a life cycle management plan.

And finally, as you can hear, there is significant excitement that PCSK9 will be a major mechanism for cardiovascular patients and we have not limited our efforts to an antibody. This year we plan to enter into the clinic with a novel small molecule that down-regulates PCSK9 and substantially down-regulates cholesterol in animals including primates. And we're also following on with a smaller molecule with a vaccine candidate that again shows remarkable data in primates, a vaccine against PCSK9 reduction and subsequent cholesterol lowering.

So a very substantial effort and we think this franchise opportunity that we are pushing forward with is an opportunity for us to be a leader and to build a portfolio with complementary positioning for patients and payers in this very large segment of cholesterol management of patients not sufficiently controlled or not suitable for statins.

Within the vaccine adult area, I wanted to give an update on our tetravalent staph aureus vaccine. It's the first of its kind that contains four vaccine components and that's important against this pathogen to generate a broad immune response. The two vaccine components on the left side, capsular polysaccharide 5 and 8 give rise, as you can see in the dark blue bars to high level of antibodies and they are sustained for up to a year. The immune response with this single injection occurs rapidly within 10 to 15 days here.

These antibodies contribute to immune elimination of the bacteria, and on the right hand you have two other immunogens that give rise to rapid onset of antibodies and these antibodies interfere with the function of the bacteria. So this multi-pronged approach is critically important for a vaccine to deal with the multi resistant staph aureus. It's a huge public health issue, we spend up to $14 billion per year, tens of thousands of patients are dying. And antibiotics are not sufficient and not suitable to control this type of difficult to treat bacteria. We are now mid of the year going to start Phase 2b. That is a pivotal study and if data is strong, we believe there are opportunities to go for dialogues around accelerated approval based on this Phase 2b study. Please note we have good experience from the meningococcal B area where we were able to get accelerated approval based on Phase 2 studies.

The additional growth platform is around the JAK platform that we have. We have now approval for RA treatment of XELJANZ in 37 countries and we recently expanded a label to importantly include prevention of structural damage. We are now launching additional indications, several of them are significant ongoing Phase 3 and you can see that they're positioned into growing beyond RA in rheumatology, the use of XELJANZ in dermatology and gastroenterology. And you will see Phase 3 readouts from UC in 15, 16 and psoriatic arthritis in 16. This year we're also filing for a once-a-day sustained release form, modified release form of XELJANZ. So that provides a real unique spectrum of the indication and dosage form for patients. I want to however to point to you that we have gotten some real important insights into the science of JAK inhibitors and how they can be modulated for disease outcome, thinking for future generation of JAKs.

So in the lower left hand, you can see that balanced profile of tofacitinib and this is what we call a spider diagram, and you can see in the periphery a number of important cytokines that are involved in autoimmune or inflammatory diseases and you can see how XELJANZ in a balanced way, partly inhibit several of them. Our efforts in this area has enabled us to design a new generation of inhibitors that now have a more narrow selective range of JAK profiles, like the JAK3 that mainly inhibits what's called the gamma chain cytokines like IL15, IL21, IL4 that are likely involved in IBD and MS, but spares cytokines such as IL10 and interferon that we believe have a protective role in IBD and MS, respectively.
Please note for some of the dermatology indications, if you look at the TYK2/JAK 1, the second to the right, you can see that we now have a more narrow profile than XELJANZ/tofacitinib but it's expanded into that IL12/IL23 segment, which is at 7 o'clock and 5 o'clock on this spider clock. And why is that important? Because we know the cytokines play a pivotal role in psoriasis as exemplified by IL12 and IL17 antibodies. So we have this unique novel generation of JAK inhibitors that can really give completely different treatment point options in autoimmune diseases. And in addition to that we have topical JAKs and inhaled JAKs for derm or respiratory condition.

Let me share with you very recent data on topical administration of tofacitinib using a unique Pfizer formulation. These are mild to moderate atopic dermatitis. You can see the baseline eczema at the top and within one week there is a dramatic reduction in itching and eczema scores whether reported by patients or physicians and within four weeks there is, in many patients a complete resolution or a very dramatic resolution of eczema.

We are now planning to start Phase 2b or Phase 3 in 2015 and 2016 with this topical tofacitinib and we are also exploring have seen some encouraging data in topical administration for psoriasis.

Gastroenterology part of inflammation, let me share with you an update on our MAdCAM antibody. This is actually the first time clinical data Phase 2b on a MAdCAM antibody has been presented. The MAdCAM antibody belongs to the broader integrin class but it's the only member of an immune modulator of this type that doesn't touch the immune system. It binds to the gut and prevents immune cells to migrate and cause inflammation. And in these ulcerative colitis studies, you can see substantial remission rates in a nice dose-dependent manner and use and given its very selective binding to the gut, the tolerability profile was very favorable and in some dimensions placebo-like.

We're now planning for a potential Phase 3 start in 2016 and I would like to point out that this profile of MAdCAM antibody with relevance for induction and maintenance gives it a very nice complementary profile for tofacitinib in a GI inflammation portfolio.

I wanted also to share with you with some of the efforts we have put over the last few years in neuroscience and pain, which has been more on the mid-term efforts versus some of the near-term I've spoken about. On one hand let me give you some encouragement on tanezumab. We were the leading company in moving anti-NGF antibodies and this is a reminder of the astonishing pain reduction data in osteoarthritis as shown by this WOMAC pain score and the level of pain reduction was significantly better than seen with any of the tested NSAIDs. There has been a class clinical hold for a couple of years from FDA concerning the need to do preclinical safety concerning sympathetic nervous system. We have concluded such extensive studies, substantial studies in primates and we are pleased to conclude that we saw a very favorable outcome of those data, and we're now starting to share the data with the FDA and pending removal or potential removal of the clinical hold, we are technically prepared to start Phase 3 studies together with our partner Lilly for osteoarthritis chronic lower back pain, as well as other pain indications.

On the right hand, we share with you data on the new chemical entity for managing pain, anxiety and possibly epilepsy around a very special GABA enhancer profile. So, these are small molecules that have unique segments of the GABA-A family that they target and spare the alpha 1 receptor. And why is that important? Well, if you look at this spider diagram, you can see the traditional benzodiazepine in red and the further out you are in the spider diagram the more response you have, but please note the boxes labeled memory, coordination, balance, and attention, are some of the difficult adverse event profile of benzodiazepines that limits their use.

And you can see how extensive lorazepam at optimal dose, one of the common benzodiazepines, hits this adverse event in the newer [cot] testing Cascade while our compounds show a nice much more narrow and cleaner profile. And then look at 12 o’clock in the spider diagram, where we have the pharmacological marker that is assumed to correlate with efficacy for anxiety or chronic pain, and see how our focused GABA enhancer actually outperforms the standard benzodiazepine. This encouraging data have stimulated us to start Phase 2 in several indications now.

And finally, I want to just to give you an update on opportunities in rare disease and this is dealing with sickle cell disease, which is one of the largest opportunities in rare disease. We had up to 80,000 patients in US alone. And sickle cell patients suffer from sickle cell crisis periods which are difficult, painful and lead to organ damage.

Together with GMI Biotech we have developed a pan-selectin inhibitor that is aimed to dissolve some of these blood clots that cause constriction of the blood flow and cost these difficult sickle cell crises. And you can see on this slide, how the treated patient group in blue, has a much shorter length of hospital stay, as a surrogate for a shorter disease suffering from the sickle cell crises. And also you can see the bullet point, we have an...
almost 90% reduction in the use of opioid to manage this painful condition. We’re advancing this now towards Phase 3 either 2015 or 2016 pending final optimization of the formulation. I hope I was able to give you real insight to the breadth of mechanism and new indications that we near term have in our portfolio and some of the transformational science that we see over the longer term.

And again it just summarizes our leadership in the CDK 4/6 arena, how we grow our immuno-oncology pipeline to aspire to be a leader in several areas, how we leverage franchise approaches in PCSK9 and JAK, and some of the mid-term opportunities in pain and hematology indications.

Thank you very much. It’s a pleasure to be here to talk to you and hopefully continue good parting dialogs, which is a very important part of the Pfizer way of moving pipeline forward with innovations and rapidly take on unmet needs among patients to accelerate medicines.

Thank you very much for your attention.

Chris Schott - JP Morgan - Analyst

Thank you. And one quick housekeeping item I forgot to mention before, and Pfizer is not going to be hosting a breakout today so I just want to give people heads up on that.

Mikael Dolsten - Pfizer Inc - President

Thank you.